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**THE MAJOR CAUSES OF FATIGUE IN PATIENTS IN THE INITIAL STAGE**  
**OF HYPERTENSION**

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In his elaboration of problems of hypertension, N. D. Strashko identified 3 phases or stages. The first is the primary or functional transitory stage; the second, the stable or organic, and the third, the terminal or dystrophic, accompanied by profound metabolic disorders and serious organic damage to organs of major importance.

The major complaint of all patients is an increasing loss of the capacity to work, a rapid onset of a feeling of exhaustion, sometimes upon the most insignificant physical effort.

With persons suffering advanced hypertension, the exceptional tendency to exhaustion is explained by functional and organic changes in the internal organs and systems -- changes complicating the course of the primary disease and markedly increasing the severity of its manifestations. In the initial phase of the disease, however, this explanation does not hold, particularly with young patients in whom, at rest, not only are symptoms of organic damage to the major systems lacking, but who frequently show no signs of functional insufficiency. Yet it is specifically this type of patient in whom the first manifestations of the disease take the form of reduced capacity to work, and extreme fatigability.

A study of the early manifestations of the disease is needed to clarify the causes of the rapid fatigability of hypertensives. The first or functional phase of the disease, characterized by unstable elevation of arterial blood pressure, has thus far been the object of comparatively little study. Having appeared only very recently (in 1952) are the discoveries resulting from the research and dynamic observation by N. V. Konovalov and E. V. Shmidt of 200 persons in the initial, transitory phase of hypertension. The present author read at a meeting of the Cardiology Institute of the Georgian Academy of Sciences in 1951 the results of a clinical and physiological study of 109 persons in the initial, functional, transitory phase of hypertension. Clinical observation showed the major symptoms in these patients to be those of instability in the regulatory function of the central nervous system. Extensive tachycardia, marked reduction in normal capacity for work, ready fatigability, interruption in and loss of sleep, along with signs of functional changes in a number of organs and systems, were more frequent and constant signs than the transitory elevation in arterial blood pressure.

At the present time we have followed more than 300 patients, up to 40 years of age, in the functional, initial phase of hypertension. Young persons with hypertension are the best source of significant data for evaluation of the special clinical features of the primary phase. Elevation of arterial pressure in such persons was of short duration, as a seemingly accidental manifestation. Study of the clinical features of the disease in such patients for 4 to 6 years showed their complaints and the objective manifestations to reduce themselves primarily to signs of excessive

excitability of the nervous system, and a complex of functional changes in the internal organs and systems, followed by a rising phenomenon of fatigue in ordinary work. The marked decline and even loss of working capacity, along with manifestations of functional insufficiency in the cardiovascular system, are the factors compelling these patients to apply for medical assistance. Almost half the persons studied revealed signs of chronic recurrent focal infection (chronic tonsillitis, periodontitis, benign endomyocarditis, etc.) Polyadenitis, pasty skin, sometimes a marked acceleration of the intradermal response to pressure, and also lymphocytosis, indicated the obvious involvement of the lymphatic system. The intradermal adrenalin test showed the skin to have a dense, extended network of lymph vessels (V. M. Primak). Signs of lymphostasis and of reduction in the depurative function of the lymphatic system may be one of the significant reasons for the organism's oxygen hunger.

In studies of the functional capacity of the cardiac muscles in persons in the primary phase of hypertension, at complete rest, the majority of the patients showed functional disturbances. The most common signs of these disorders on auscultation are unusual relationships between the heart sounds, the first being somewhat dulled and the second intensified, while the sounds may also be separated or repeated. In functional stress, more than 3/4 of the patients reveal an increase in the clarity with which this repetition may be distinguished. Here, as V. P. Obratsov put it, "we have...a whole scale of states, gradually progressing one from the other, in which the heart, beginning with an innocent, hardly detectable repetition of a sound, proceeds to a clearly pathological

stage: a cardiac gallop." If the fact be taken into consideration that persons in the initial phase of hypertension often report angina pectoris, while electrocardiograms after exercise, orthostatics, or developing pyrexia reveal indications of coronary insufficiency, one must regard these apparently purely functional cardiac disorders to be of the highest significance as signs of disorder in the regulatory function of the nervous system over the myocardium. I. P. Pavlov, demonstrating the existence of special cardiac trophic nerves, in addition to functional nerves regulating the activity of the cardiac musculature, and vascular nerves governing the variable inflow of blood thereto, speaks of 3-fold nervous control of the heart.

The signs of transient toxic myocarditis in our patients are related to disorders in trophics. This provides proof that functional disorders in the myocardium were more constant and stable than elevation of arterial blood pressure. Consequently, even in the primary phase of hypertension, the control of the nervous system over trophic processes in the heart is violated.

However, elevation of arterial blood pressure is a secondary and less stable phenomenon than functional changes in the cardiac muscle.

Changes in the cardiovascular system in the first phase of hypertension were also characterized by the irregularity of function of the capillaries. In 20% of patients this instability manifested itself in an exceptional redness of the skin, sudden erythemas, and constant dermographia (which may even take the form of urticaria). In 80% of patients, capillaroscopy, particularly

under conditions of thermal stress, revealed clear signs of stable capillaropathy.

Elevated permeability of the vascular membranes and, therefore, frequent swelling of the perivascular connective tissue, susceptibility to various catarrhs, and elevated reactivity to common stimuli, all testify interference with the regulatory function of the nervous system in the functional stage of hypertension.

Almost half our patients complained not only of rapid fatigability but of increasing dyspnea of greater or lesser duration. In addition to this subjective sign of decline in the respiratory function of the lungs, almost 1/3 of our patients revealed a decline in vital capacity, sometimes combined with frank fluxion (according to F. G. Yanovskiy). Decline in intensity of sound on percussion, weakened respiration of indeterminate character, and crepitative and subcrepitative rales in the lower portions of the lungs (particularly to the right posteriorly), while exceedingly inconstant and transitory, nevertheless frankly reflected the disorders in the respiratory functions of the lungs which facilitated the development of hypoxia.

We followed the method of I. M. Sechenov in studying the oxygen and carbon dioxide content in the venous blood of 85 persons with functional hypertension. The work was usually done during the first days of the patient's visit to the clinic and again before he was discharged. In some cases the test was run 3, 4, or 5 times. This study showed 57 persons to have venous hypoxemia (i.e., less than 10% by volume of oxygen in the venous blood). Arterial hypoxemia (less than 17% oxygen by volume) was found,

however, only in 10 persons. At the same time, 56 persons showed signs of elevated oxygen content (more than 20% by volume) in the arterial blood. A marked increase in the difference in oxygen between arteries and veins (over 10% by volume) was found in 51 persons.

The extraordinary instability, or, to be more exact, the high lability of hypoxemic change testifies, in our opinion, to the insufficiency of the regulatory function of the nervous system, which is responsible for the exceptional fatigability of hypertensives.

Table 1 illustrates the marked fluctuations in the gas composition of the blood in 3 patients suffering primary hypertension. The oxygen content of the venous blood shows the more marked fluctuation. The percentage saturation of this blood with oxygen declines in certain individuals to extremely low levels (30%).

Thus, profound disorders are revealed in those functions of the central nervous system which regulate the constancy of the optimal oxygen composition in the tissues of the organism under conditions of complete rest. They are particularly marked under various functional stresses. The hypoxia revealed also explains the elevated fatigability of hypertensives.

The disturbance in the regulatory function of the nervous system could also be found in our patients in study of carbohydrate metabolism. In 25 patients in the primary, transitory stage of hypertension, the sugar level was determined on an empty stomach and then after 50 ml of glucose had been taken enterally. These

determinations were repeated every half-hour for 2 to 2.5 hours (researcher: Budnitskaya). In this way, the majority of the patients tested were found to show some decline and lag in hyperglycemic elevation. Administration of glucose to patients kept in an oxygen tent for an hour (80% oxygen) had a marked effect on the glycoemia curve in almost 2/3 of those studied.

[See Table 1, following page.]

By way of illustration, we adduce the data on patients F-na, 25, Case History 1591, and P-k, 26, Case History 885.

	F-na		P-k	
	Without O <sub>2</sub>	With O <sub>2</sub>	Without O <sub>2</sub>	With O <sub>2</sub>
Empty stomach	82	94	83	107
30 minutes after 50 ml				
glucose	126	160	124	168
60 minutes after 50 ml				
glucose	78	128	118	142
90 minutes after 50 ml				
glucose	89	100	96	115
120 minutes after 50 ml				
glucose	78	82	88	121

Noting the rise in the glycoemia curve in oxygen therapy, we cannot refrain from the thought that the improvement in the regulatory function of the nervous system and the subsequent normalization of the processes of metabolism is affected by the O<sub>2</sub>.

The clinical manifestations of the primary forms of hypertension (those which N. D. Strazhesko classified as the 'initial, functional, transitory stage of the disease') testify that in this

TABLE 1  
BLOOD GASES IN PATIENTS IN THE PRIMARY STAGE OF HYPERTENSION

Name, age, sex	Date		Cases in Blood							
			Arterial		Venous		Difference between arterial and venous		% saturation	
			O <sub>2</sub>	CO <sub>2</sub>	O <sub>2</sub>	CO <sub>2</sub>	O <sub>2</sub>	CO <sub>2</sub>	arterial	venous
G-n, 18, male	1/25	140-70	22.87	41.35	8.28	48.2	14.59	6.65	98	35
	2/2	125-65	20.11	43.39	12.27	50.04	7.84	6.65	94	58
R-k, 28, male	4/30	160-106	20.76	39.08	6.7	46.48	14.16	7.1	90	30
	5/28	-	18.91	41.15	12.12	45.06	6.79	3.4	87	87
Th-s, 26, male	6/3	125-75	24.91	37.07	11.73	47.92	13.18	10.88	97	42
	6/21	130-75	21.9	41.52	11.52	47.56	10.48	6.04	94	49

stage there is a significant change in the reaction of the organism to the external and internal environment.

Studies of metabolism (water, salt, protein, and carbohydrate), determination of the reactions of the vascular system (fluctuations in arterial and venous pressure), and of shifts in the function of the capillaries (including changes in the permeability of vascular and perivascular membranes), investigations of gas metabolism (basal, carbon dioxide, and oxygen in arterial and venous blood), and also of peculiarities in the respiratory function of the lungs, of cardiac activity, and of renal function, always reveal deviations from the regularity observed in the healthy organism. The absence of such regularity in metabolism in general, and particularly in oxygen metabolism, is the immediate cause of fatigue in the primary, purely function stage of hypertension.

G. V. Pol'bort, analyzing problems of fatigue, gave particular emphasis to the role of long-continued or intensive activity by various organs as the basic cause of insufficiency in their function.

In clinical practice only individual aspects of this are seen, peculiar to each patient. But the most frequent and significant cause, reducing the functional capacity of the cardiovascular system, is hypoxia.

Clinical practice demonstrates that the most characteristic sign of the onset of hypertension is not elevated arterial blood pressure, but extreme instability thereof, as well as exceptional lability of other functions of the sick organism, reflecting the degree of distortion of the regulatory function of the central

nervous system. This is why such great significance is attached to a proper judgment of the state of the patient at the very beginning of the development of this disease, as emphasized by N. D. Strazhesko. F. A. Andreyev writes of this: "The onset of illness, the transition from healthy to diseased state — the most critical moment in life — is something which we physicians omit from consideration." Yet the most important moment at the onset of hypertension is the rising feeling of fatigue when ordinary work is performed.

Systematic study of the most important functions of the organism in the initial phases of hypertension testifies the importance of patients' complaints about fatigability. It is specifically in the functional stage of hypertension that one can follow the disruption of the correct relationships between the functions of the cerebral cortex, the vegetative nervous system, and the internal organs.

Here we are not concerned with the developed picture of hypertension with its permanently elevated arterial pressure and consequent complications. But we note that the extreme lability of the regulatory function of the central nervous system with regard to the processes of metabolism, and functional disorders in the most important organs and systems, cause the manifestations of the initial phase of hypertension to resemble the clinical signs of its advanced stage. The degree of functional disorder, and the stability therein have, as we see, serious significance in evaluation of the actual condition of the patient even during the period when arterial blood pressure may remain essentially normal, but the results of oxygen insufficiency are already evident.

G. V. Vel'hort and his pupils, studying the processes of fatigue in various organs, showed that there was a regular connection between the processes of expenditure and recovery. Exhaustion facilitates the development of the inhibitory process. The inhibitory process not only interrupts the functional destruction of cells; it stimulates the restoration of its exhausted reserves. But under pathological conditions, cases may be encountered in which these regular relations are violated, i.e., the process of exhaustion does not induce a process of inhibition, and the process of inhibition ceases to be the stimulus to recovery. This violation is observed in the most varied forms in hypertensives, with their complaints of extreme fatigability and elevated reactivity of the nervous system.

While noting the elevated excitability and rapid exhaustion of the central nervous system, we are not always able to identify their causes.

A. L. Myasnikov, speaking of the fact that disorders in the higher nervous activity represent the foundation of hypertension, in which stagnant centers of excitation take form in the cerebral cortex and subcortical region, nonetheless emphasizes that these disorders result "primarily under the influence of external factors." Our clinical experience leads us to identify 2 types of external circumstances which govern the development of hypertension: focal infection and developing hypoxic changes. True, our clinical observations provide an adequate number of examples of the fact that the unfavorable effects both of infection and of hypoxemic shifts upon the organism are themselves conditioned by the same weakening

and reduction in the regulatory function of the central nervous system. However, the total influence of these conditions of the external environment, leading to repeated exacerbation of focal infection and increasing and sometimes highly stable evidences of hypoxia, was so well-defined in more than half the cases we studied that they (chronic infection and hypoxia) have to be regarded as the most common unfavorable external environmental conditions, development of which leads to the extreme fatigability of persons suffering hypertension.